Laparoscopic Versus Open Appendectomy
A Prospective Randomized Double-Blind Study

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Summary Background Data: The value of laparoscopy in appendicitis is not established. Studies suffer from multiple limitations. Our aim is to compare the safety and benefits of laparoscopic versus open appendectomy in a prospective randomized double blind study.

Methods: Two hundred forty-seven patients were analyzed following either laparoscopic or open appendectomy. A standardized wound dressing was applied blinding both patients and independent data collectors. Surgical technique was standardized among 4 surgeons. The main outcome measures were postoperative complications. Secondary outcome measures included evaluation of pain and activity scores at base line preoperatively and on every postoperative day, as well as resumption of diet and length of stay. Activity scores and quality of life were assessed on short-term follow-up.

Results: There was no mortality. The overall complication rate was similar in both groups (18.5% versus 17% in the laparoscopic and open groups respectively), but some early complications in the laparoscopic group required a reoperation. Operating time was significantly longer in the laparoscopic group (80 minutes versus 60 minutes; $P = 0.000$) while there was no difference in the pain scores and medications, resumption of diet, length of stay, or activity scores. At 2 weeks, there was no difference in the activity or pain scores, but physical health and general scores on the short-form 36 (SF36) quality of life assessment forms were significantly better in the laparoscopic group. Appendectomy for acute or complicated (perforated and gangrenous) appendicitis had similar complication rates, regardless of the technique ($P = 0.181$).

Conclusions: Unlike other minimally invasive procedures, laparoscopic appendectomy did not offer a significant advantage over open appendectomy in all studied parameters except quality of life scores at 2 weeks. It also took longer to perform. The choice of the procedure should be based on surgeon or patient preference.

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Key Words: appendicitis, appendectomy, laparoscopy

Since its initial description by Semm[1] in 1983, laparoscopic appendectomy (LA) has struggled to prove its superiority over the open technique. This is in contrast to laparoscopic cholecystectomy, which has promptly become the gold standard for gallstone disease despite little scientific challenge.[2] Open appendectomy (OA) has withstood the test of time for more than a century since its introduction by McBurney[3]: the procedure is standardized among surgeons and, unlike cholecystectomy, OA is typically completed using a small right lower quadrant incision and postoperative recovery is usually uneventful. It is the second most common general surgical procedure performed in the United States, after laparoscopic cholecystectomy, and the most common intraabdominal surgical emergency, with a lifetime risk of 6%. The overall mortality of OA is around 0.3%; and morbidity, about 11%.[4] Given the large number of procedures done annually, the validation of a minimally invasive technique that would improve outcomes may have a direct impact on patient management and possibly an indirect effect on the economics of health care.

Numerous prospective randomized studies,[5–26] meta-analyses,[27–30] and systematic critical reviews[31–34] have been published on the topic of LA, with a general consensus that the heterogeneity of the measured variables and other weaknesses in the methodology have not allowed to draw definitive conclusions and generalizations.[33,34]

With this in mind, we have designed a prospective randomized study (PRS) comparing LA to OA that included double blinding of the patient and the independent data collector, a factor missing in all but 2 PRS.[11,23]

MATERIALS AND METHODS

Inclusion Criteria

Patients with appendicitis were included in the study performed at Los Angeles County and the University of

Southern California Medical Center (LAC+USC Medical Center). The diagnosis of appendicitis was made on the following criteria:

History of right lower quadrant pain or periumbilical pain migrating to the right lower quadrant with nausea and/or vomiting, fever of more than 38°C and/or leukocytosis above 10,000 cells per mL, right lower quadrant guarding, and tenderness on physical examination.

All patients included were 16 years of age or older.

Exclusion Criteria

Patients were excluded if the diagnosis of appendicitis was not clinically established and if they had a history of symptoms for more than 5 days and/or a palpable mass in the right lower quadrant, suggesting an appendiceal abscess treated with antibiotics and possible percutaneous drainage. Patients with the following conditions were also excluded: history of cirrhosis and coagulation disorders, generalized peritonitis, shock on admission, absolute contraindication to laparoscopic surgery (large ventral hernia, history of laparotomies for small bowel obstruction, ascites with abdominal distension), contraindication to general anesthesia (severe cardiac and/or pulmonary disease), inability to give informed consent due to mental disability, and pregnancy.

Randomization

The qualifying patients were informed of the risk and benefits of each operation and asked to sign a detailed informed consent in their respective native language, approved by the institutional review board (IRB).

Baseline evaluation of the following parameters was performed before randomization once the informed consent was signed: measurement of pain on a visual analog scale (VAS) and measurement of activity using a scoring system.

Computer-generated random numbers were used to assign the type of surgery (laparoscopic or open), which were written on a card sealed in a completely opaque envelope.

Surgery

Residents performed all operations with 4 attending surgeons experienced in open and advanced laparoscopic techniques. The level of expertise in the performance of the standardized LA technique was verified by the senior author (NK) before the beginning of the trial.

Patients received 1 g of cefoxitin every 8 hours intravenously from the time of diagnosis until surgery. Patients found to have a complication (gangrenous or perforated appendicitis) during surgery were treated with "triple antibiotic" coverage: ampicillin (patients allergic to penicillin received vancomycin), gentamycin, and metronidazole until the white blood cell count was within normal limits and the temperature under 37.9°C for 24 hours. All other patients did not receive any antibiotics postoperatively. No urinary catheter was used. Nasogastric tubes were inserted in patients

suspected to have a significant postoperative ileus. OA used a McBurney muscle-splitting incision 1.5 inches in the right lower quadrant. A double ligation of the stump was performed with an absorbable suture. If the appendix looked normal, it was removed, and the distal ileum was visualized to detect possible Meckel's diverticulitis. The abdomen and pelvis were irrigated with warm saline solution. The skin incision was closed with 3-0 nylon (Ethilon; Ethicon, Somerville, NJ). In the case of a perforated appendix, the skin wound was closed loosely.

LA was performed using 3 ports, with the laparoscope positioned at the umbilicus. Two 10-mm ports were inserted in the right and left lower quadrants. The abdominal cavity was explored to locate the appendix and rule out other possible diagnoses. The appendix and the mesoappendix were divided with an Endolinear Cutter 45 with blue and vascular staples, respectively (Ethicon Endosurgery, Cincinnati, OH). The right lower quadrant, the right colic gutter and the subhepatic space in the case of purulence were irrigated and the fluid was suctioned. The appendix was removed in a laparoscopic bag. Fascial defects in the port sites were closed using 0 Vicryl suture. The skin incisions were closed in every case using 3-0 nylon. Nonsuction drainage was left in situ in cases of abscess and residual cavity.

Blinding

At the end of each procedure, 3 wound dressings and an abdominal binder were applied to every patient to blind the patient, the nursing and the medical staff, and the independent data collector as to the nature of the procedure.

Postoperative Course

Strict criteria were followed for the reintroduction of nutrition. Bowel sounds were checked every 12 hours. Once present, the patients were started on a clear liquid diet and advanced to regular diet when the liquid diet was tolerated and flatus observed. Patients were discharged when they tolerated a regular diet, had a normal white blood cell count under 10,000/mL, and were afebrile for 24 hours.

Outcome Parameters

The following parameters were recorded:

• Anesthesia time in minutes from the time of induction to reversal and operating time skin to skin in minutes.

• Indications for conversion from LA to OA.

• Complications (intraabdominal abscesses were defined by the presence of fever and elevated WBC and evidenced by computed tomography; wound infections were defined as redness and drainage from the wound requiring opening of the skin incision and packing).

• Pathology based on reports (acute, gangrenous, or perforated appendicitis).

• Time until resumption of diet (clear liquid and regular diet) in hours and hospital stay in days.

• A 13-item Activity Assessment Scale was used to measure activity on every postoperative day. This measured the patient's ability to perform 13 activities: lying in bed, sitting, getting in or out of bed or chair, reaching or stretching activity, lifting 3 to 5 pounds, walking around inside, climbing up and down stairs, walking outside or at work, sedentary activities, light physical activities, moderate physical activities, vigorous activities, sexual activity. All items had response categories scaled from 1 through 5, with verbal descriptors for each item. The response categories for activity were (1) no difficulty at all; (2) a little difficulty; (3) some difficulty; (4) a lot of difficulty; (5) not able to do it. The Activity Assessment scale is the sum of the 13 items, with higher scores indicating poorer activity.

• Postoperative pain was assessed in 2 ways by the data collector blinded to the type of operation: *quantitatively* by daily tabulation of medication requirements (a standardized postoperative regimen was given to all including Tylenol/codeine capsules as a first line of treatment and shots of IM Demerol as needed). Pain and discomfort were also assessed *qualitatively* using 2 items: a pain distress variable and a pain activity scale. The pain distress variable was a single response item that the patients used to indicate on a visual linear scale the severity of the worst pain that they experienced in the preceding 24 hours. The item was scaled from 0 to 100, with 0 being no pain and 100 being the most intense pain imaginable.

• The pain activity scale assessed pain during 3 activities, namely, (1) rest, (2) normal daily activities, and (3) exercising or during strenuous work. The patient's response to the 3 levels of activity was assessed using a visual linear score with a scale of 0 to 100, with 0 being no pain sensation and 100 being the most intense pain imaginable.

• At 2 weeks, patients were seen in the wound clinic and checked for complications (wound infection, intraabdominal abscess formation, and any other complication). Qualitative pain scores, activity, and quality-of-life scores were completed. Quality of life was measured with the SF-36. The SF-36 (Medical Outcomes Trust, Boston, MA) is a validated, multipurpose, short-form health survey with only 36 questions. It yields an 8-scale profile of scores: physical functioning (PF), role-physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role-emotional (RE), and mental health (MH). Each item has response categories describing the level of functioning of the patient from normal to severely impaired, as well as physical and mental health summary measures. They represent the most frequently measured concepts in widely used health surveys. It is a generic measure as opposed to the ones that target a specific age, disease, or treatment group. It has been constructed to satisfy minimum psychometric standard measures for group comparisons.

• Accordingly, the SF-36 has been accepted as valid health measures for descriptive purposes, such as documenting differences between sick and well patients and for estimating the relative burden of different medical conditions. It has been documented in more than 1000 publications involving more than 130 diseases and conditions.

• Readmissions to the hospital and their cause were also recorded.

Statistical Methods

The appropriate sample size for our study was calculated before the beginning of the trial based on an analysis of sample sizes required for each of the main parameters (operating time, diet, length of stay, return to normal activity) for an $\alpha = 0.05$ and a power of 90%.

All comparisons between groups were intention-to-treat analyses in which patients were analyzed according to the assigned treatment group. Conversions to open were therefore analyzed in the laparoscopic group. Statistical analyses of quality-of-life outcomes and the quality-of-pain assessments were evaluated using the differences between the open group and the laparoscopic group with respect to the change from preoperative scores for each time point. The change in scores for the SF-36 QOL form, the activity assessment scale, the pain activity scales, and the pain distress score was compared using Wilcoxon rank-sum tests separately for each time point. The χ^2 test was used to compare proportions.

There were missing data in 10 patients in the laparoscopic group. To exclude any bias and to determine the effect of the missing data, a second analysis was performed in which we inputted values equal to the 25th percentile for all the responding patients in that group. The inputted values were set for the worst and best possible scenarios, and a reanalysis was performed. In all but 2 cases, the second analysis produced results similar to the primary analysis. The exceptions were with regard to time of oral intake of liquid and solid foods. When the inputted values for time to oral feeding were set to the worst level, there was a statistically significant difference in the time to oral intake of liquids in the favor of the laparoscopic group. When the inputted values were set to the best possible score for the oral intake, there was a statistical difference in the time to oral intake of solid and foods, which also favored the laparoscopic group. In particular, even if we assumed that all the patients with missing data in the laparoscopic group had a complication, a secondary analysis revealed no significance difference in the complication rate between the 2 groups ($P = 0.122$).

All continuous variables are expressed as median (interquartile range). All *P* values reported are 2-sided, and $P < 0.05$ denotes statistical significance.
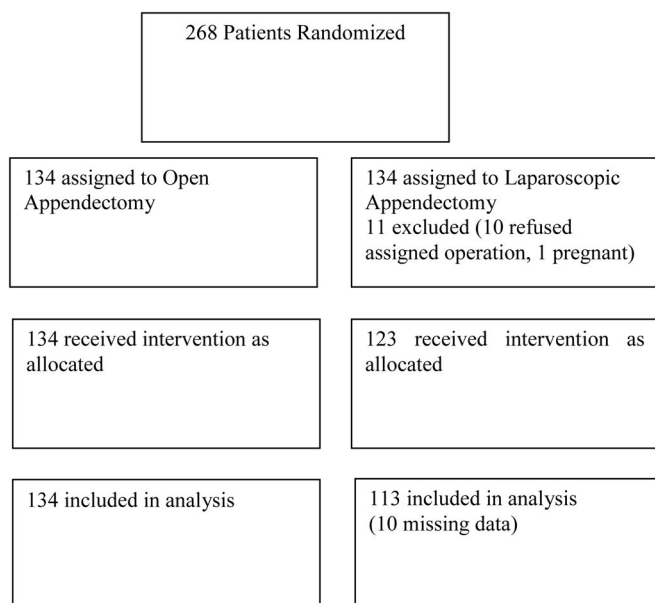
FIGURE 1. Patient allocation.

TABLE 2. Complications

Laparoscopic Group (n = 21)	Open Group (n = 23) (P = NS)
Enterocutaneous fistula 1 (required reop)	Wound dehiscence 1
Postoperative bleeding 3 (required reop)	Intraoperative cecal perforation 1
Wound infections 7	Wound infections 9 (P = NS)
Intraabdominal abscess 6	Intraabdominal abscess 4 (P = NS)
C diff colitis 1	Right hemicolectomy 1
Ileus 2	Intraoperative bleeding (500 mL) 1
Phlebitis 1	Right femoral nerve palsy 1
	Unknown fever 2
	Ileus 3

RESULTS

Two hundred sixty-eight patients were randomized to either laparoscopic or OA. Eleven were excluded from the study (10 refused treatment assignment and 1 was pregnant; see Fig. 1). There were missing data in 10 patients; therefore, 247 were available for the analysis.

Demographics

The 2 groups were similar with respect to age, sex, and preoperative white cell count (Table 1).

Morbidity

There was no mortality in this study. There was no significant difference in the overall complication rates (18.5% in the LA group versus 17.1% in the OA group) (P = 1.00) (Table 2).

Four major complications in the laparoscopic group required a reoperation: 3 postoperative bleedings from an injury to the inferior epigastric artery from the left lower quadrant trocar and the other from the appendiceal artery. An enterocutaneous fistula was the result of an unrecognized monopolar electrocautery injury to the terminal ileum during a straightforward LA for acute appendicitis. Patient developed extensive cellulitis on the first postoperative day, and the reintervention required a cecal resection. All 4 patients had an uneventful recovery. In the open group, none of the complications required a reoperation; the patient with wound dehiscence was treated conservatively. The occurrence of a right femoral nerve palsy was unexplained, but the patient recovered spontaneously. In 1 patient, a right hemicolectomy was performed for to a large suspicious cecal wall mass. The pathology confirmed its benign nature.

There were no differences in infectious complications between the laparoscopic group (7 wound infections and 6 intraabdominal abscesses) and the open arm (9 wound infections and 4 intraabdominal abscesses). There were also no significant differences in the wound infection rates (6.2% versus 6.7%; P = 1.00) and the abdominal abscess rates (5.3% versus 3%; P = 0.51) between the LA and the OA respectively (Table 2). All patients with intraabdominal abscesses were readmitted and treated successfully with antibiotics and CT-guided drainage when the collection was encapsulated.

TABLE 1. Patients Characteristics*

Characteristics	Assigned to Open Appendectomy	Assigned to Laparoscopic Appendectomy	Open vs. Laparoscopic
Number	134	113	
Age (y)	28 (17–63)	29 (18–71)	P = 0.39
Men	104	78	P = 0.13
WBC preop	15.4 (12.2–17.9)	15.4 (13.4–18.3)	P = 0.28

*Results as median IQR.

TABLE 3. Clinical Outcomes*

	Assigned to Open Appendectomy	Assigned to Laparoscopic Appendectomy	Open vs Laparoscopic
Operative time (min)	60 (45–75)	80 (60–105)	$P = 0.000$
Anesthetic time (min)	95 (75–115)	125 (105–152)	$P = 0.000$
Time to liquids (h)	24 (20–42)	23.5 (10.5–32.5)	$P = 0.10$
Time to solids (h)	38 (24–51)	27 (20–48)	$P = 0.37$
Parenteral analgesics, # doses	2 (1–5)	2 (1–4)	$P = 0.716$
Oral analgesics, # doses	2 (0–6)	2 (0–4)	$P = 0.502$
Length of stay (days)	3 (2–4)	2 (2–4)	$P = 0.66$

*Results as median IQR.

Clinical Outcomes (Table 3)

The operative time and the total anesthetic time were significantly longer in the laparoscopic group. Nine patients in the laparoscopic group were converted to an open procedure (8%). The indications for conversion were inability to insufflate in 1, unclear anatomy or difficult dissection in the remaining 8. There was no difference in the time to resumption of liquids or solid food between the 2 groups. The length of hospitalization was the same for both groups.
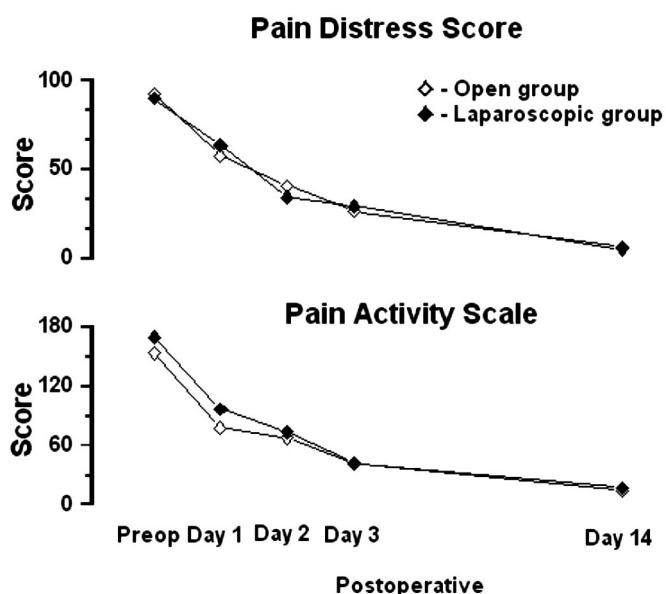
Seventy-five percent (185/247) of patients were discharged on or before day 3.

Pathology

There were 6 normal specimens (1 in the OA and 5 in the LA group), 139 acute appendices (78 in the OA and 61 in the LA group), and 86 complicated with gangrene or perforation (49 in the OA and 37 in the LA group). Information was absent in 16 cases (6 OA and 10 LA). No significant differences were noted between the 2 procedures (0.153). Appendectomy for acute or complicated (perforated and gangrenous) appendicitis had similar complication rates regardless of the technique ($P = 0.181$).

Postoperative Pain (Tables 3 and 4)

Preoperatively, the severity of pain experienced and its influence on activity were similar for both groups (Fig. 2).

TABLE 4. Qualitative Pain Assessment (VAS) and Activity Scores*

	Assigned to Open Appendectomy	Assigned to Laparoscopic Appendectomy
Pain distress		
Preop	92 (70–100)	89.5 (54–100)
Day 1	57.5 (37–83)	63.5 (23–85)
Day 2	40.5 (17.5–71.5)	34 (20–73)
Day 3	26 (7–48)	29 (9–50)
2 wk	6 (0–24)	5 (0–10)
Pain activity score		
Preop	153 (100–200)	169 (120–200)
Day 1	77 (48–133)	96 (55–137)
Day 2	67 (40–106.5)	73 (38–104)
Day 3	41 (17–88)	41.5 (15–109)
2 wk	14 (23–54)	16.5 (3–40)
Activity assessment		
Preop	50 (39–60)	48 (37–56)
Day 1	52 (47–55)	54 (23–56)
Day 2	50 (47–55)	50 (46–53)
Day 3	56 (53–60)	55 (53–59)
2 wk	37 (28–44.5)	37 (27–46)

VAS indicates visual analog scale.
*Results as median IQR.

FIGURE 2. Qualitative pain assessment.

Postoperatively, both groups experienced a similar severity of pain on postoperative days 1, 2, 3, and at 2 weeks. Narcotic medication usage to control postoperative pain was also equivalent between the 2 groups. There was no significant difference between the total number of parenteral doses of narcotics or the number of doses of oral analgesics used between the 2 groups. The impact of the patient's pain and its limitation on various daily activities were again similar throughout the postoperative period (Fig. 2).

Activity (Table 4)

There was no difference between the 2 groups with respect to the performance of routine daily activities and the limitation imposed by the surgery on such activities on day 1, day 2, day 3, and at 2 weeks postoperatively (Fig. 3).

Quality of Life (Table 5)

At 2 weeks postoperatively, quality of life as assessed by the SF-36 form was administered to 114 patients. It showed a significant difference for 2 out of 8 domains (physical functioning and general health). There was also a significant difference between the 2 groups with regard to the temporal changes in the physical health score and general score at 2 weeks compared with preoperatively (Fig. 4). The changes in mental health score were similar for both groups.

DISCUSSION

Our study demonstrates that LA is comparable to OA in all studied outcome parameters, except for an advantage at 2 weeks in certain aspects of quality of life. LA took longer to perform.
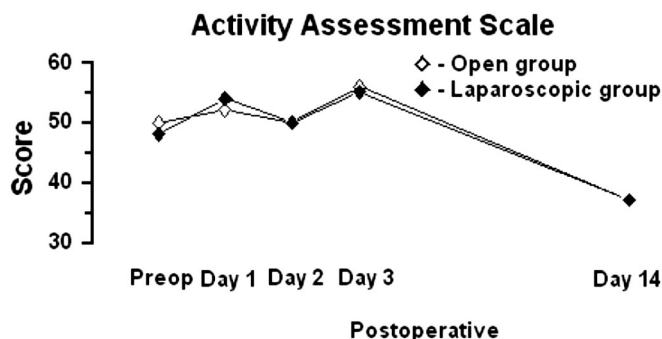
Review of the Methodology

The failure of a minimally invasive procedure to improve results significantly over a century-old operation led us to caution in the interpretation and validation of the data. We performed an extensive search strategy to include the most relevant body of literature comparing laparoscopic to OA in adults using the review of Cochrane Central Registry of Controlled Trials, MEDLINE, and SciSearch. Among the

TABLE 5. SF-36 Preoperatively and at 2 wk*

	Open Appendectomy	Laparoscopic Appendectomy
Physical functioning		
Preop	29 (20–30)	18.5 (14–28)
Postop	22 (16–27)	24.5 (18–28)
Role physical		
Preop	19 (15–20)	16.5 (12–20)
Postop	11 (8–15)	12 (8–16)
Bodily pain		
Preop	3 (2–5)	4 (2–6)
Postop	4 (3–6)	5 (4–6)
General health		
Preop	17 (14–18)	16.5 (9–18)
Postop	14 (10–17)	15 (13–17)
Vitality		
Preop	12 (11–13)	12 (11–13)
Postop	13 (10.5–14)	12 (11–13)
Social functioning		
Preop	6 (6–6)	6 (5–6)
Postop	6 (5–6)	6 (5–7)
Role emotional		
Preop	14.5 (11–15)	13 (9–15)
Postop	12 (9–13)	12 (9–15)
Mental health		
Preop	17 (15–18)	17 (15–18)
Postop	17 (16–18.5)	17 (15–18)
Physical health score		
Preop	64.5 (54.5–69)	52.5 (46–65)
Postop	51 (43–59)	55 (47–62)
Mental health score		
Preop	47 (42–51)	46.5 (41–50)
Postop	46 (41–50)	46 (41–50)
SF36 score		
Preop	113 (98–118)	100 (89–111)
Postop	66 (59–78)	72 (63–80)

*Results as median IQR.

large number of publications, 45 prospective randomized studies (PRS) were analyzed. Twenty-two adhered to acceptable methodology and were retained.[5–26] In addition, 4 meta-analyses,[27–30] 4 systematic reviews (including 1 Cochrane database),[31–34] and 4 large nonrandomized comparative trials were included in our review.[4,35–37]

As suggested by all meta-analyses and systematic reviews, the methodological quality of most studies was "poor to moderate."[33] Only 7 PRS had a sample size of 200 patients or more.[10,12,17,18,20,23,24] Some papers published in the early 1990s enthusiastically proclaimed the superiority of LA but included less than 80 patients in both groups.[5,7]
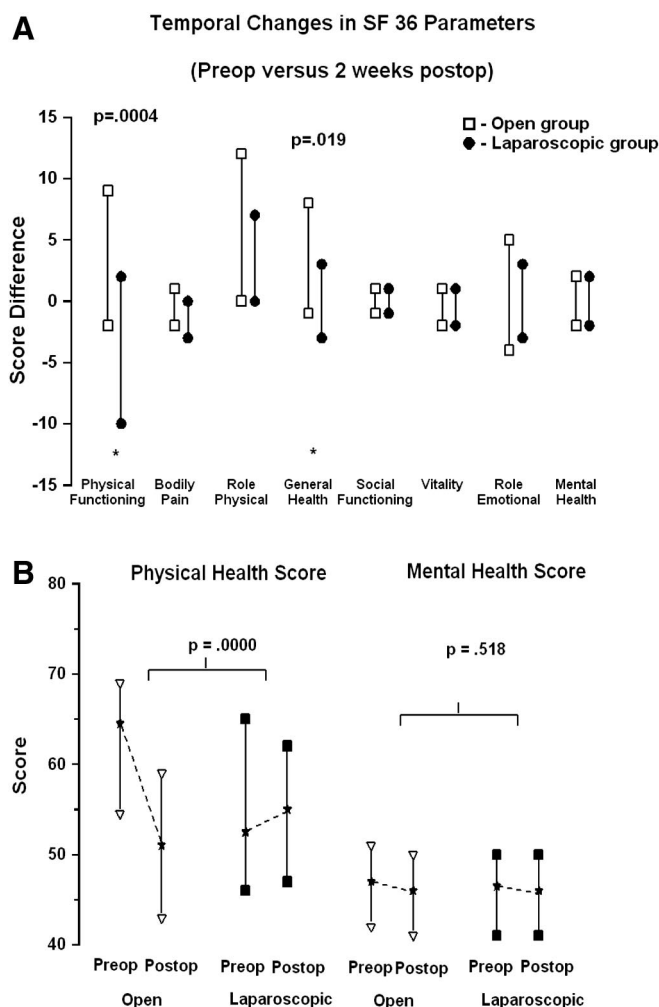

FIGURE 3. Activity assessment scale.

FIGURE 4. Assessment of quality of life (SF-36).

One PRS drew conclusions from 50 patients.[21] The merit of these early studies was their attempt to evaluate a new operative technique, but definitive conclusions cannot be drawn.

The majority of comparative nonrandomized studies favored laparoscopy. These should be analyzed with great caution because of their inherent bias.[35–37] In 1993, Tate et al[36] from Hong Kong published data collected on the initial 55 patients 6 months after the introduction of LA in their hospital that were compared retrospectively to 100 OA. They found significant benefits in favor of LA. These same authors in a follow-up PRS conducted in the same institution concluded that their study could "no longer support the widespread adoption of a laparoscopic alternative to a traditional operation based on initial enthusiastic but uncontrolled studies."[26]

Two studies from Sweden and Denmark that included 500 and 583 patients, respectively, are the largest PRS to date.[10,24] Both studies followed sound scientific principles, but the lack of appropriate blinding and the inclusion of multiple centers weakened the results. The participation of 85 surgeons in the Swedish study introduced wide variability.

Only a fraction of the PRS analyzed data based on intention-to-treat principles (ITT).[6,10,14,22,24] The absence of ITT can lead to a bias towards laparoscopy as the more complex cases may have been converted to open.[6]

To analyze the rate of intraabdominal abscess formation, we calculated that 2514 patients would have had to be included to achieve significance. Chung et al[27] found that based on a true difference of 1% and each rate being less than 5%, 4200 patients are required to be randomized to achieve a power of 80%. This constitutes an impractical task. The aim of meta-analysis studies is to overcome this hurdle and to draw conclusions based on available data. Meta-analysis has its intrinsic weakness: pooled results add biases from each of the individual studies. In fact, in one study, the rate of accurate prediction of 12 large randomized trials by meta-analyses was 35%.[38] Slim et al[34] critically reviewed laparoscopic surgery trials. Among the 40 PRS analyzed, half were considered poor, and those on appendectomy were the poorest. Their inclusion in a meta-analysis would result in type 1 and/or type 2 errors.

Blinding of patients, caregivers, and the data interpreters is a very important factor when studying subjective variables such as pain assessment. Also, in the absence of masking, the duration of hospital stay can be markedly influenced by the enthusiasm for a novel technique. The critical importance of blinding was clearly demonstrated by Majeed et al[2] in a study comparing laparoscopic versus open minicholecystectomy. It showed no difference between the 2 methods in all the subjective variables measured. Our trial was unique because we conducted a double-blinded study in which the patient had an abdominal binder, thus blinding the patient, surgical team, and the independent data collector to the technique employed. Only 2 other studies included blinding.[11,23] In one, blinding was only used to administer the visual analogue pain scale in a subgroup of 134 patients of the 253 randomized.

We conducted the study in 1 center (LAC+USC Medical Center), and 4 surgeons, all with excellent open and advanced laparoscopic expertise, attended all cases performed by residents at the level of PGY2 and above. The laparoscopic technique was standardized before randomization, and no deviation was allowed during the study. This was all done to improve the homogeneity of the results.

In summary, we found that some papers concluded with the superiority of one procedure (generally laparoscopy) over the other based on small statistical differences that might not be clinically relevant. In an analysis of 12PRS, Slim et al[34] found 6 negative studies in which small sample size and lack of power limited their value. The agreement in the 6 positive

trials was reported only on subjective parameters, and these studies suffered from methodological flaws due to lack of blinding.

Review of Outcomes

There was no mortality in our study. This is consistent with the majority of past publications. The overall reported mortality of appendectomy is very low and was estimated in a review of a large administrative database at 0.05% for LA and 0.3% for OA,[4] reinforcing the fact that appendectomy in the absence of peritonitis is a safe procedure, regardless of the technique performed. Our complication rates were similar in both groups. This is similar to most randomized studies, reviews, and meta-analyses (Table 6). It is significant, though, that the most serious early complications occurred in the laparoscopic group and required a reoperation: an injury of the epigastric vessels due to an inadequate trocar placement occurred in one of our patients. This is a well-known complication noted by others and avoidable with the placement of trocars under direct vision lateral to the epigastric arteries and the use of newer nonbladed trocars (Optiview, Ethicon EndoSurgery). The removal of all cannulas should also be done under direct vision prior to releasing of the pneumoperitoneum to detect any subtle bleeding from the abdominal wall. The most serious complication in the laparoscopic group was an enteric leak manifested through the trocar wound on the first postoperative day. This was due to an unrecognized burn injury at the antimesenteric side of the terminal ileum. The reoperation required a limited cecectomy. The use of monopolar electrocautery should be limited in a straightforward LA, especially in the obese patient or in the case of difficult visualization.

Infectious complications represented by wound infections and intraabdominal abscesses are 2 variables by which the techniques have been traditionally compared. Wound infections may not be serious complications per se but represent a major inconvenience to the patient, impacting his convalescence time and quality of life. Intraabdominal abscess formation is a serious complication and can potentially be life threatening. We found that the incidence of wound infections was similar in both groups. This is in contradiction with the majority of studies (Table 6). On the other hand, Klingler et al,[13] in a study focused on the assessment of infectious complications in a PRS, corroborated our results, as the incidence of wound infections in their study was 6%

TABLE 6. Summary of 4 Meta-analyses

	Sauerland, 1998[30]	Chung, 1999[27]	Garbutt, 1999[28]	Golub, 1998[29]
# PRS included	28	17	11*	16
N	2877	1962	?	1682
OR time (diff)	Lap > Open (+16 min)[†]	Lap > Open (+31.4%)[†]	Lap > Open (+17 min)[†]	Lap > Open (+17 min)[†]
Overall complications	Lap = Open	N/A	Lap = Open	Lap = Open
Wound infections (diff)	Lap < Open (−4.2%)	Lap < Open (−4.3%)[†]	Lap < Open (−3%)[†]	Lap < Open (−4%)[†]
Intraabdominal infections (diff)	Lap > Open (+0.9%)	Lap > Open (+1%)	Lap > Open	Lap > Open (+1%)
Pain	Lap < Open[‡]	Lap < Open[†]	Lap < Open[†‡]	Lap < Open[†]
Length of stay (diff)	Lap < Open (−15 h)	Lap = Open	Lap = Open	Lap < Open[‡]
Return to full activity (diff)	Lap < Open (−7 d)	Lap < Open (−6.2 d)[†]	Lap < Open (−5 d)[†]	Lap < Open (−5.1 d)[†]
Lap advantages	Less wound infection	Less pain	Less wound infection	Less wound infection
	Earlier recovery	Less wound infection	Less pain	Less pain
		Earlier recovery	Earlier recovery	Earlier recovery
Lap disadvantages		Longer operation	Higher cost	Trend toward more intraabdominal infections
Conclusions	Flaws in methodology do not allow for generalization	Flaws in methodology	Trend favoring lap but only 4/8 parameters were significant	Widespread use of lap should be considered

Diff, difference; Lap, laparoscopic; OR, operating room; PRS, prospective randomized studies.
*All intention-to-treat analysis.
[†]$P < 0.05$.
[‡]On postoperative day 1.

and 7% in the laparoscopic and open groups, respectively. In one of our cases, the breakdown of the extraction bag may have contributed to the wound infection. Three other cases with wound infections were among those patients in the laparoscopic group that were converted to OA. The intraabdominal abscess rate was slightly higher in the laparoscopic group, but the difference did not reach a statistical significance, possibly because of insufficient sample size (type 2 error). This is consistent with the literature[27–30,33] (Table 6). We have previously shown that it is possible to reduce the incidence of intraabdominal pelvic abscesses if the sigmoid colon is retracted, the patient placed in Trendelenburg, and the pelvis is completely irrigated and aspirated under direct vision.[39] This maneuver was not systematically performed in our study, as it was not part of the standardized operative protocol. Regardless of the technique employed, the increased incidence of intraabdominal abscess following LA is concerning, especially when performing the procedure for perforated appendicitis. Some authors have advocated the open technique in this indication.[40]

The operating room time was longer in the LA group. We measured both anesthesia and the actual skin-to-skin time. We did not find any study demonstrating a shorter time for LA, despite the subjective perception that it can be an easier operation. This may be due to the inclusion of additional steps for setup, insufflation, trocar entry under direct vision, and diagnostic laparoscopy. We did not evaluate the cost of both procedures, because of the economic setting at the Los Angeles County Medical Center, where most of the patients are uninsured and hospital charges are global. However, the longer operating time, in addition to the cost of the disposable equipment used, may increase the direct cost of LA.

Pain assessment was studied in 2 ways: subjectively by the administration of a visual analogue scale test and objectively by the tabulation of pain medications. There was no difference between the 2 groups. The literature is divided on this subject. Some studies show less pain in the first 2 days after laparoscopy.[27–30,33] All but one of these studies[23] were nonblinded, thus reducing the validity of the results. Others have confirmed our findings.[11,21,22]

The length of hospital stay in our study was short, and there was no significant difference between the groups. This finding is similar to others.[27,28] Early publications in the 1990s demonstrated a significantly shorter hospital stay in favor of LA,[5,7] yet perhaps this is one area where OA has caught up with the laparoscopic techniques. Lord and Sloane[41] showed that a 48-hour discharge policy for OA could be implemented with the appropriate staffing infrastructure. Longer hospital stays in European studies could be the consequence of different social standards and insurance systems.[10,12,20,22]

In our study, the blinding of our patients and nurses and the adherence to strict discharge criteria can be a factor

explaining the absence of difference between the groups. The lack of blinding can introduce bias towards laparoscopy because the patients and the caregivers are motivated toward an earlier discharge.

The return to activity following appendectomy is the subject of intense debates. A minimally invasive operation (LA) by definition should allow for a quicker recovery, shorter convalescence at home, and quicker return to work. Our results based on the use of an objective instrument to measure the activity showed no difference in scores postoperatively and at 2 weeks. Others found improved postoperative activity (Table 6), but the interpretation and the comparison among the studies are difficult because of the variable definitions of activity. Results in all 4 meta-analyses were statistically "highly heterogeneous." In contrast, Ignacio et al[11] carried out a blinded prospective study in a tertiary care military-based hospital on healthy active-duty men. This specific cohort was selected because the mandatory documentation required for convalescence in the military made for accurate assessment of lost days. In this study, there was no difference in pain on days 1 and 7 postoperatively or in the time to return to work. We did not use the return to work as an end point, given the confounding heterogeneity of employment and insurance coverage among our patients.

The assessment of quality of life using the SF-36 showed improved scores in the laparoscopic group for 3 of the 8 parameters, namely, physical functioning, general health, physical health, and in the general score. Our study is unique as no other work on appendicitis has used this validated tool. It is also possible that the lack of late blinding might have influenced the results.

Our study has some limitations. We could not assess the effects of laparoscopic surgery in the obese patient, as body mass indices were not recorded. As mentioned above, cost analysis was not included, and our follow-up was limited to the first 2 weeks postoperatively. Our aim was to rule out early postoperative complications after hospital discharge and assess activity and quality of life on the greatest number of patients. Finally, our study population was predominantly of Hispanic ethnicity and may not be representative of the general population in the United States.

In conclusion, LA is not superior to OA. It is an equivalent technique as the benefits gained through improved quality of life were offset by the effect of longer operating times and more serious early complications.

Some authors praise the value of laparoscopy in the case of diagnostic uncertainty among women.[16] This application may not be as useful in the current age of widespread use of CT scans with excellent specificity and sensitivity for the diagnosis of appendicitis.[42]

LA has been demonstrated to have advantages in certain situations such as surgery in the obese patient.[43] Im-

proved cosmesis by hiding trocar incisions in the pubis can be an advantage for certain patients.[24]

The reduction of adhesion formation following LA as shown by de Wilde[44] could possibly affect the long-term incidence of small-bowel obstructions following appendectomy. Finally, LA provides a safer training model for young residents to hone their laparoscopic skills than laparoscopic cholecystectomy.

Based on what we know today, we recommend that the choice of the procedure be based on surgeon or patient preference.

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Discussions

Dr. Adrian Barbul (Baltimore, Maryland): The group from USC led by Dr. Katkhouda has carried out an outstanding study comparing open versus laparoscopic techniques for appendectomy. Merits of the study include its randomized blinded design, the small and homogeneous group of well-trained surgeons participating in the study, the comprehensive in-hospital and post-discharge analysis and assessment, and the intent to treat statistical analysis, which is the most stringent and meaningful of all. The authors find that there were no differences in outcome parameters and propose that the therapeutic approaches to this common surgical problem should be left to the surgeon and to the patient's choice. I have a few comments and questions.

Number one, although the number of complications did not differ among the groups, life-threatening complications requiring reoperation occurred only in the laparoscopically treated group. Does this not mean that the approach is more risky?

Two, in light of the longer OR and anesthesia times and most likely increased supply costs, can the hospital CFO or the department chair allow the choice of the procedure to be made by the surgeon or patient? I am sure the third-party payers will adopt this study as a way to limit payment for the laparoscopic procedure. Although you did not pursue an economic analysis of the two procedures, does the lap approach make economic sense?

Most laparoscopic approaches have gained acceptance because of decreased length of stay, decreased time to recovery, faster return to work, and decreased analgesic requirements. These parameters were not different in the appendectomy study that you carried out. Is this a reflection of "the minor nature" of the procedure of appendectomy? I ask you to comment on that.

Finally, you only found a difference in the two techniques when applying the SF-36 tool, and how are we to judge the significance of those differences and do they justify the laparoscopic approach?

Dr. Namir Katkhouda (Los Angeles, California): The first question is definitely provocative: Is laparoscopic appendectomy a more risky procedure? Even though we have indeed in the laparoscopic group three patients that had bleeding that required the reoperation and one patient in which I was personally involved that presented an enterocutaneous fistula that had to be brought back to the OR the next day, I cannot say today that it is a more risky operation. I would say this to answer this question: When laparoscopy goes well, everything goes well. When it goes bad, it really goes bad as opposed to open. In other words, if there are any complications they usually are more serious and they will require reoperation.

The second question involves the cost of the procedure. In our setting at County Hospital with the special population we have, mostly uninsured patients, we were not able to do a cost analysis. But I understand the question based on the longer OR time and anesthesia time. Time is money in the OR. And if you add the cost of OR time to the disposable equipment, one can probably foresee an increased direct cost.

Now, I am not sure about the indirect costs. Again, we did not look at the return to work. But if we look at what was published in the literature, we can see that there is indeed about a $2,000 savings if one does an open operation.

So is it cost-effective to do open or is it more costly to do lap? It is tough to say. It remains that in a teaching institution, laparoscopic appendectomy still remains a good training model for young residents in training before going to a bigger operation, such as even lap chole.

The fact that we did not find any differences in pain or other measured variables, is it due to the nature of the small operation, quote/unquote, because of the small incision? Of course some will compare the three-and-a-half inch trocar incision to the 3-cm McBurney. Well, we saw the same problem with the hernia. When you compare a laparoscopic to an open procedure using small incisions, it is always difficult to find differences. Is it a minor operation? No. One should remember that this operation could be useful in the obese patient and could also be useful in young women in child-bearing age.

Finally, how do you evaluate the three parameters that we found as significantly different in the quality of life measurement? Again, those are small differences. It joins what we have found in the literature about a slight improvement in the activity or quality of life following lap. But it cannot make the operation a much better operation. We are convinced that both operations are comparable despite the slight difference because what is gained in improved quality of life is lost in a larger operation and potentially more serious complications.

Dr. Michael S. Nussbaum (Cincinnati, Ohio): Is it your conclusion that in young men in which you can be fairly certain that they have appendicitis that there is no difference between the open and laparoscopic approaches? My question is: How many patients had to be excluded because of diagnostic uncertainty? Isn't that really where the benefit of laparoscopy is? If you are uncertain of the diagnosis, particularly in a young woman, you can obtain a much better evaluation of the abdomen when a laparoscopic approach?

You didn't look at cost, therefore my other question is: You assume that the cost of extending the surgical time and the disposables used in the laparoscopic cases are greater. However, to be diagnostically certain that you are dealing with appendicitis does that mean that a CT scan must be obtained more frequently in those patients and wouldn't that be an additional cost for the open group?

DR. NAMIR KATKHOUDA (LOS ANGELES, CALIFORNIA): I cannot answer this question because I do not have the number of patients who were in the situation of diagnostic uncertainty. But I understand the problem in young women.

In the day and age of CT scanners, currently in our hospital there is very little room for diagnostic uncertainty clinically. I think when we are in a situation where you have diagnostic uncertainty, we order a CT scan. And that usually in more than 90% will clarify the problem.

So I will agree that in young men with appendicitis, laparoscopy and open are comparable procedures. The jury is still out for young women. Some studies show a benefit in women in favor of laparoscopy. We were not able to really prove that.

DR. ALAN G. JOHNSON (SHEFFIELD, ENGLAND): I am delighted to see that you adopted our original design of blinding the patients and nurses by putting the same dressings on the abdomen after both operations.

What did you tell the patients beforehand about when they could go home? Expectation has a great effect on patients' behavior.

Secondly, did you really use a "classic McBurney" incision? That is a high, oblique incision. I do not think the young woman would have thanked you for that. Do you not mean a low crease incision?

Thirdly, how often did you have to extend the open incision beyond the one inch (2.5 cms)? Did you compare these two groups? The problem is that the position of the appendix can vary.

Finally, when you found a normal appendix, did you take it out or leave it alone?

DR. NAMIR KATKHOUDA (LOS ANGELES, CALIFORNIA): When we unblinded the patient, told them to go home, we actually urged them to go back to activity as soon as possible.

The second question was about the incision, how many times did we have to enlarge the incision and did we look at stratifying the results based on the larger incision?

Finally, the incision was a classic McBurney incision. We did not do any cosmetic operations. We just wanted an incision that would fit all.

DR. LEIGH A. NEUMAYER (SALT LAKE CITY, UTAH): It appears that you used the Activity Assessment Scale and the Visual Analogue Scale that we had developed for the hernia studies, and I congratulate you on that and encourage anyone in the audience who is doing surgical studies and who wants to look at outcomes, that those are now well-validated measures. They will be published in *The Journal of American College of Surgeons* in the next couple of months. You can pick them up there or e-mail me. For my question: The SF-36 that you used postoperatively, did you use the acute version or just the regular version?

DR. NAMIR KATKHOUDA (LOS ANGELES, CALIFORNIA): We used the same activity scores that you used and published recently in *The New England*, so I thank you for your inspiration. Having said that, we used a regular SF-36.

DR. JACQUES PERISSAT (BORDEAUX CEDEX, FRANCE): Your conclusion seems to be too straightforward, having a lack of nuances. It is choking my convictions. You know very well that in Europe we have some such studies, maybe not so rigorous and scientifically based as you have done. Our conclusion is very similar, except for two categories of patients.

The first category is the group of young female adults in full sexual activity for two reasons. The first one is because laparoscopy can secure better the diagnosis of acute appendicitis regarding the frequency of confusing gynecologic disorders in that kind of patient. The second reason is also the great concerns of those patients about the final cosmetic results of the operation.

The second category is the group of patients having a possible but not quite obvious clinical feature of diffused peritonitis, especially in obese people. For them the open route obliges frequently to enlarge the opening of the abdominal wall with great damaging consequences. Using the laparoscopic approach can avoid such drawbacks.

I have two questions. The first one is: have you made a selection among your female patients with regards to their sexual status?

The second is: How have you rejected patients with clinical features of diffuse peritonitis?

My third additional question would be: Have you created special new tricks in open surgery to avoid the sometime necessary enlargements of the opening of the abdominal wall?

DR. NAMIR KATKHOUDA (LOS ANGELES, CALIFORNIA,): I think the first question was asked before (benefit of laparoscopic appendectomy in young women). We did not randomize based on sex or age. We just randomized every patient who qualified.

As for peritonitis, these patients were clearly excluded in our study. I agree that there could be some benefit of washing out the patient laparoscopically in the presence of peritonitis, but those patients were excluded in the study.

And finally, I don't have any more tricks than what my mentors taught me back in France while doing open appendectomies. I used the classic McBurney incision.